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			1639	

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/791,977

Applicant(s)

CHEN ET AL.

Examiner

Sue Liu

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 6/3/04.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) 7 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☒ Claim(s) 5 is/are objected to.
- 8) ☒ Claim(s) 1-7 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. <u>20060922</u> .                           |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application  |
| Paper No(s)/Mail Date <u>3/2/04</u> .  | 6) <input type="checkbox"/> Other: _____                           |

## DETAILED ACTION

### *Claim Status*

Claims 1-7 are currently pending;

Claim 7 has been withdrawn;

Claims 1-6 are being examined in this application.

### *Election/Restrictions*

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group 1. Claims 1-6, drawn to a method of microwave-assisted protein array fabrication, classified variously, for example in class 436, subclass 518.

Group 2. Claim 7, drawn to a full automatic protein array system, classified variously, for example in class 435, subclass DIG 48.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions of Groups I and II are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another and materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case, the method of Group I method can be made by hand printing proteins on the slides and manually carry out the attachment reactions, which would not require the automatic protein system (or apparatus) of Group II invention. Thus, restriction between the groups is proper.

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3. Therefore, these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and/or recognized divergent subject matter. Even though some of the groups are classified in the same class/subclass, this has no effect on the non-patent literature search. The different methods and products will require completely different searches in both the patent and non-patent databases, and there is no expectation that the searches will be coextensive. Therefore, these do create an undue search burden, and restriction for examination purposes as indicated is proper.

#### *Applicants' Election*

4. During a telephone conversation with Thomas Schneck on 7/14/06 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-6. (See the attached Interview Summary). Affirmation of this election must be made by applicant in replying to this Office action. Claim 7 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicants also elected "aldehyde slide" as a species of slides during the same telephone conversation on 7/14/06.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

5. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

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application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Priority***

7. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. (Foreign priority paper: Taiwan 92115883; 6/11/03).

### ***Claim Objections***

8. Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The instant Claim 5 is dependent on Claim 1, which recites the limitation of "a slide of aldehyde surface" used in the instant claimed method. However, the instant Claim 5 recites different type of slides including "aldehyde surface slides, poly-L-lysine coated slides, epoxy coated slides, and FAST slides (SS, nitrocellulose)". Thus, the subject matter of the instant Claim 5 is broader in scope than that of the instant Claim 1, and Claim 5 is not further limiting the subject matter recited in Claim 1.

### ***Claim Rejections - 35 USC § 112***

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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10. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase “which is characterized in that the printed array is immobilized...” (the last two lines of the instant Claim 1), which is unclear and confusing. It is not clear if the last two lines of the instant Claim 1 are part of the claimed method steps. It is also not clear if the “microwave irradiation” technique is part of the claimed method of fabricating protein array. The recitation “accelerates the blocking reaction by microwave irradiation” is also unclear and confusing. It is not clear if the “microwave irradiation” technique is part of the blocking reaction procedure or if it is an additional step.

Claim 1 recites the phrases “PBSM (skim milk in PBS buffer, w/v 2%)” and “PBST (Tween 20 in PBS buffer, w/w 0.025%)”, which is confusing because it is not clear the terms in the parentheses are examples of the terms “PBSM” and “PBST” or they recite the definitions for the said terms. It is also not clear to which ingredient(s) in the buffers the terms “w/v 2%” and “w/w 0.025%” are referring.

Claim 4 recites the phrase “the time to accelerates the blocking reaction is 1 to 5 minutes”, which is unclear and confusing. The instant claim language can be interpreted to mean that the blocking reaction is conducted in 1 to 5 minutes, or that the blocking reaction is accelerated by 1 to 5 minutes. The different interpretations would result in different time ranges such as any time periods for the latter interpretation, and thus rendering the claim indefinite.

Claim 1 recites the limitation “the proteins” in line 2. There is insufficient antecedent basis for this limitation in the claim.

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Claim 1 recites the limitation "the blocking reaction" in lines 3 and 9. There is insufficient antecedent basis for this limitation in the claim.

Claim 1 recites the limitation "the detection procedure" in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claim 1 recites the limitation "the printed array" in line 8. There is insufficient antecedent basis for this limitation in the claim.

Claim 2 recites the limitation "the microwave intensity" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 3 recites the limitation "the immobilization time" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 4 recites the limitations "the time" and "the blocking reaction". There are insufficient antecedent bases for these limitations in the claim.

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

(Note: the instant claim numbers are in bold font.)

12. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ault-Riche et al (US 2002/0137053 A1; 9/26/2002), in view Martin et al (US 2003/0082633 A1; 5/1/2003;



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filed 9/5/2002), Schleifer et al (US 2003/0231989 A1; 12/18/2003; filed 6/14/2002), Jacob et al (US 2002/0095073; 7/18/2002), and Duhamel et al (Journal of Histochemistry and Cytochemistry. Vol. 33 (7): 711-714; 1985).

The instant claims recite a method of microwave-assisted protein array fabrication, comprising the steps of:

printing the proteins on a slide of aldehyde surface to produce a protein array, immersing the protein array in PBSM (skim milk in PBS buffer, w/v 2%) for the blocking reaction,

washing with PBST (Tween 20 in PBS buffer, w/w 0.025%),

rinsing with PBS buffer, and dry with centrifugation and proceed to the detection procedure or preserve by refrigeration;

which is characterized in that the printed array is immobilized by microwave irradiation, and accelerates the blocking reaction by microwave irradiation.

As discussed above in the rejection under 35 U.S.C. 112, second paragraph, the claim language (Claim 1) is unclear and confusing. It is not clear if the recited microwave irradiation is part of the "printing" process. It is also not clear if the terms in parentheses are examples or components of the terms "PBSM" or "PBST". Furthermore, it is also not clear to which ingredients the term "w/v 2%" and "w/w 0.025%" are referring. It is herein interpreted as referring to 2% non-fat milk and 0.025% Tween-20 for the purpose of the following rejection. The instant Claim 4 is also not clear as discussed above, and the claim can be interpreted to mean any time period.

Ault-Riche et al, throughout the publication, teach methods of generating protein arrays (See Abstract of the reference). The reference teaches generating protein arrays comprising antibodies (p. 2, [0014]), and various other proteins such as peptides, and antisera reactive (p. 6, [0062]), which reads on the protein array of **clm 1**, and the different proteins of antibody, antigen and substrates as recited in **clm 6** because the instant disclosure does not specify the terms "antigen" and "substrates" (which can be any protein). The reference also teaches that the solid

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support for the protein array can be glass slides (p. 6, [0060]), which reads on the slide of **clms 1 and 5**. The reference also teaches attaching proteins onto superaldehyde slides or membranes containing aldehyde groups so that the aldehyde groups can react with primary amines in the protein to form covalent linkages between the supports and the proteins (p. 23, [0247]), which reads on the aldehyde coated slides of **clms 1 and 5**. The reference teaches using PBS containing 0.05% Tween-20 as blocking and washing solutions (p. 30, [0317]) and using PBS to rinse the protein array (p. 30, [0319]), which reads on the PBST washing and PBS rinsing steps of **clm 1**. The reference also teaches using 3% non-fat milk in buffer for blocking the protein array (p. 35, [0368]), which reads on the skim milk for the blocking reaction in **clm 1**. The reference also teaches conducting detecting assay using the array (p. 24, [0258]-[0259]), which reads on the detection procedure of **clm 1**.

Ault-Riche et al do not specifically teach using microwave irradiation for immobilization and accelerating the blocking reaction as recited in **clm 1**. The reference also does not explicitly teach using centrifugation to dry the slides, and using refrigeration to preserve the protein array as recited in **clm 1**. The reference also does not explicitly teach 2% skim milk in PBS for blocking reaction, and 0.025% Tween-20 for washing solution as recited in **clm 1**. The reference also does not specifically teach the immobilization time is 30-90 seconds, and the blocking reaction accelerated by 1 to 5 minutes.

However, Martin et al, throughout the publication, teach using microwave to accelerate chemical reactions such as those used in protein chemistry (see Abstract of the reference). The reference teaches using microwave with frequencies of 2.45GHz (p. 6, [0108]) and is the frequency used in conventional microwave oven (p. 1, [0006]), which reads on the intensity of

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**clm 2.** The reference also teaches the microwave-generated heat energy accelerates a desired chemical reaction on the surface of the target object (p. 1, [0003]). The reference also teaches the preferred surface is glass slides (p. 11, [0149]), and microwave can be used to attach molecules such as proteins onto a surface (p. 10, [0139]), which reads on the immobilization (or attachment) of protein to the slides of **clm 1**. In addition, the reference teaches that the microwave assisted reaction can be virtually any chemical reaction in which the reactant(s) can be bound to a specific binding reagent (p. 10, [0138]). The reference also teaches the reactions can be binding reactions between proteins (p. 11, [0143]). Because the “blocking” reaction is essentially a non-specific protein binding reaction as taught by Ault-Riche et al (p. 30, [0317] of the Ault-Riche reference), the reactions that can be accelerated by microwave heating taught by Martin et al encompass non-specific protein binding to the substrates.

Schleifer et al, throughout the publication, teaches multiple array substrates that comprise arrays such as polypeptide arrays (see Abstract and p. 1, [0004] of the reference). The reference also teaches using centrifugation to dry the slides that comprise the array (p. 13, [0083]), which reads on the “dry with centrifugation” of **clm 1**. The reference also teaches by centrifugation the slides can be dried in 3 min (p. 13, [0083]).

Jacobs et al, throughout the publication, teaches methods of making and using microarrays that comprise proteins using aldehyde-derived glass (Abstract and p. 19, [0213]). The reference also teaches the unused slides can be stored under refrigeration (p. 17, [0195]), which reads on the refrigeration step of **clm 1**. The reference also teaches the need to refrigerate biological samples (p. 15, [0169]).

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Duhamel et al, throughout the reference, teach using nonfat milk to block nonspecific protein binding (see Abstract of the reference). The reference teaches using 2.5% and 5% nonfat milk in buffered saline and using non-fat milk in PBS buffer (p. 711, right col., para 2; p. 722, left col., para 3). The reference also teaches nonfat milk is effective as a blocking agent and has broad usefulness (Abstract of the reference).

Although all of the above listed references do not explicitly teach 2% skim milk concentration in the buffer solution, and 0.025% Tween-20 concentration in PBS, it is prima facie obvious for a person of ordinary skill in the art at the time the invention was made to optimize the concentrations of these blocking agents in the buffer solutions to achieve best experimental results. See MPEP 2144.05; II Optimization of Ranges, A. Optimization Within Prior Art Conditions or Through Routine Experimentation:

“Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 (“The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.”); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).”

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Although the above references do not explicitly teach the immobilization time is 30 to 90 seconds, and the blocking reaction is 1 to 5 minutes, it is an inherent property of the microwave oven (or a device that can emit microwave intensity or frequency of 2.45GHz) to heat reactants and form the reactions in the said time range. See MPEP 2112.02 Process Claims:

“Under the principles of inherency, if a prior art device, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art device. When the prior art device is the same as a device described in the specification for carrying out the claimed method, it can be assumed the device will inherently perform the claimed process.”

The above references (e.g. Martin et al) teach using microwave with frequency of 2.45GHz (a microwave oven) to accelerate chemical reactions. The instant claims recite using microwave with intensity or frequency of 2 to 3 GHz, which is the same device as the one taught by Martin et al. Thus, the device (microwave oven) taught by Martin et al is capable of performing the method described (i.e. heating the reactants to immobilize proteins and block binding in 30 to 90 seconds and 1 to 5 minutes respectively).

Therefore, it would have been prima facie obvious for a person of ordinary skill in the art at the time the invention was made to using microwave assistance to print proteins onto aldehyde surface and then block with the appropriate blocking reagents such as milk and Tween-20 in buffered saline (such as PBS).

A person of ordinary skill in the art would have been motivated at the time of the invention to use microwave with frequency of 2.45GHz (microwave oven) to carry out various binding reactions with proteins, because Martin et al teach the advantages of using microwave

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such as acceleration of chemical reactions, and microwave assisted reaction is widely applicable as discussed above.

A person of ordinary skill in the art would have been motivated at the time of the invention to use centrifugation to dry protein arrays on slides, because Schleifer et al teach the advantages of using centrifugation for drying such as the short drying time of 3min as discussed above.

A person of ordinary skill in the art would have been motivated at the time of the invention to refrigerate unused slides that comprise proteins, because Jacobs et al teach the need to refrigerate biological materials (such as proteins) and the unused microarrays as discussed above.

A person of ordinary skill in the art would have been motivated at the time of the invention to use non-fat milk contained in buffered saline such as PBS buffers to block non-specific bindings, because Duhamel et al teach the advantages of using non-fat milk as a blocking reagents such as its effectiveness as a blocking agent and its broad usefulness as discussed above.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications because using microwave to accelerate reaction is routine and known in the art as demonstrated by Martin et al, printing or immobilizing proteins onto aldehyde derived slides are also known and routine in the art as demonstrated by Ault-Riche et al, blocking non-specific protein binding with non-fat milk and Tween-20 is also routine and known in the art as demonstrated by Ault-Riche et al and Duhamel et al, and the various other

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procedures for using and making protein arrays including drying with centrifugation and refrigeration are all known and routine in the art as taught by Schleifer et al and Jacobs et al.


***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached at 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL  
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9/27/2006

  
MARK SHIBUYA, PH.D.  
PATENT EXAMINER